REMARKS

In response to the final Office Action dated September 10, 2002 continued examination is requested under 37 C.F.R. 114. The present amendment, an accompanying information disclosure statement without copies of references (the references will be obtained and filed as soon as possible) and a terminal disclaimer are filed for further prosecution.

I. Claims 8 to 14

Non-elected claims 8 to 14 have been canceled without prejudice as requested in the final Office Action. Claim 8 was the main allowed claim in the parent application.

II. Obviousness Rejection of Claims 1 to 7 based on Prior Art

Claims 1 to 7 continue to be rejected under 35 U.S.C. 103 (a) as obvious over Embase Abstract -272 in view of WPIDS abstracts -924 and -225 and all the references of record in U.S. Patent Application Ser. No. 08/738,314.

The references, DE 42 24 534 A1 and DE 41 04 385 C1, were of record in U.S. Patent Application 08/738,314. These DE references disclosed closest prior art methods to the methods of claims 1 to 7. Claims 1 to 7 have not been canceled, but a new independent claim 15 has been filed, which includes the features of amended claims 1 to 3.

Claim 15 emphasizes important features of preferred embodiments for

combination preparations including preferred natural estrogens and preferred natural and synthetic gestogens.

Claim 1 of U.S. Patent 6,133,251 was allowed on the basis of the evidence in the Declaration filed with the amendment dated March 12, 2002. The results in the Declaration show that the method claimed in that claim 1 is more effective in preventing conception than that of the two DE references, but at the same time significantly reduces intercyclic bleeding.

These results also provide a basis for allowing applicants' amended claims 1 to 7 and new claim 15.

The problem that the invention of the applicants solves is to provide an effective contraceptive preparation with at least reduced side effects, which contains natural estrogens instead of ethinyl estradiol. The preparations including ethinyl estradiol had a number of disadvantages as explained in the background section, but until the applicants' work no effective preparation based on natural estrogens had been made. Previous attempts failed because the preparations with the natural estrogen caused too much intracyclic bleeding.

Thus the most important feature of the invention is the selection of only natural estrogens for use in the various stages, instead of synthetic estrongens, such as ethinyl estradiol. It is surprising that this replacement can be performed without causing too much intercycle bleeding, as the results reported in the Declaration show. The various other differences, such as division of the second stage into two parts, are secondary.

Furthermore the particular natural estrogens recited in the specification

and in the claims, such as new claim 15, are inter-converted in the body, so that administration of one estrogen leads to amounts of the other estrogens being produced, in many cases. For example, estradiol is metabolized into estrone. This transformation step occurs in the intestinal tract, the liver and many of the important target tissues, such as uterine tissue. Also the reverse reaction, the metabolism of estrone to estradiol is a well-established phenomenon.

The sulfination of estrone and estradiol at C3 is of great quantitative importance. This step is reversible as the attached scheme shows. Thus oral administration of estrdiol leads to a huge "pool" of estrone-3-sulfate in circulation. The ongoing hydrolysis of a substantial portion of this pool leads to generation of estrone. Conversion of the formed estrone to estradiol produces large amounts of this estrogen in the blood and target tissues. An information disclosure statement listing references supporting these facts is also being filed.

For these reasons broad claims that recite a first and third stage including administration of natural estrogen are reasonable without limitation to particular estrogens, simply because the various individual estrogens are inter-converted in the body. Of course the relative amounts of the estrogens may be influenced by shifts in chemical equilibrium, when one or more is administered.

This suggests that claim 1 of the above-identified U.S. Patent Application should be allowed from the same reasons as claim 1 of U.S. Patent 6,133,251, although it is somewhat broader.

For the foregoing reasons and because of the comparative experimental

results filed in the accompanying Declaration, withdrawal of the rejection of amended claims 1 to 7 under 35 U.S.C. 103 (a) as obvious over Embase Abstract -272 in view of WPIDS abstracts -924 and -225 and all the references of record in U.S. Patent Application 08/738,314 is respectfully requested.

III. Obviousness-Type Double Patenting Rejection

Claims 1 to 7 were rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1 to 7 of U.S. Patent 6,133,251.

A timely filed terminal disclaimer accompanies this amendment to overcome this obviousness rejection.

Because of the accompanying timely filed terminal disclaimer withdrawal of the rejection of claims 1 to 7 under the judicially created doctrine of obviousness-type double patenting over claims 1 to 7 of U.S. Patent 6,133,251 is respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawing be further amended or corrected in formal respects to put this case in condition for final allowance, then it is requested that such amendments or corrections be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing the case to allowance, he or she is invited to telephone the undersigned at 1-631-549 4700.

In view of the foregoing, favorable allowance is respectfully solicited.

Respectfully submitted,

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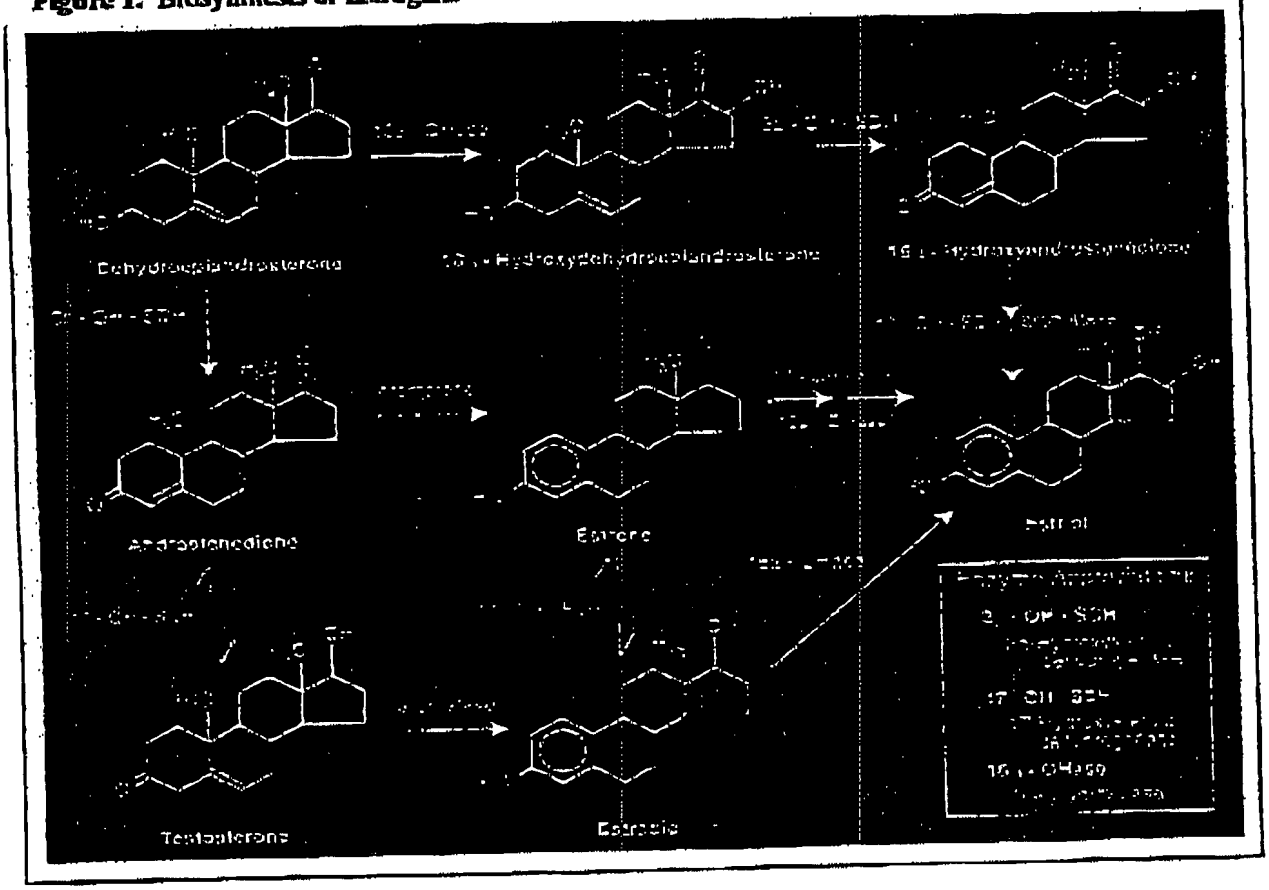
...e: scheme

Figure 1. Biosynthesis of Estrogens



Wright JV, Schliesman B, Robinson L: "Comparative measurements of serum estriol, estradiol, and estrone in non-pregnant, premenopausal women; a preliminary investigation". Altern Med Rev (United States), Aug 1999, 4(4) p266-70, *Figure 1. Biosynthesis of Estrogens*

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